REMARKS/ARGUMENTS

Claim status. Claims 3, 4, 5, 7, 8, 9, 25, and 26 are now in the case. Claims 3, 7, 8, 9, 25, and 26 are amended. Claims 1, 2, 6, and 10 to 24 have been canceled. No claims are added hereby.

Response to objection regarding sequence rules. The Examiner suggested that applicants define the Xaa at specific locations in Markush language for the Xaa substituents.

The sequence listing rules explicitly do not apply to the situations for which the Examiner is requesting a sequence listing. As noted in 37 CFR Section 1.821, "Sequences with fewer than four specifically defined nucleotides or amino acids are specifically excluded from this section. 'Specifically defined' means those amino acids other than 'Xaa'...." The Applicants have complied with this rule and cannot be compelled to go beyond its terms.

Moreover, the Sequence Listing rules reflect how one will supply sequences for subject matter disclosed; they do not limit the subject matter that one may regard as an invention. As noted in their previous response, the Applicants did not supply sequence listings for subject matter that did not fall within the Sequence Listing requirements. Furthermore, the variable length substituents would not aid the Examiner in examining the claimed subject matter.

New matter rejection under Section 132(a). In this rejection, the Examiner is objecting the use of "Δ" (Greek letter delta) at page 42, line 26 to page 43, line 6. Here, the Examiner is plainly mistaken, perhaps due to reliance on a web version of the application. According to the files held by the Applicants' attorney, the application as filed includes "Λ" (Greek letter lambda) to indicate the presence of a linker. The objected symbol was in the application as filed and was not added by amendment. Thus, the new matter rejection has no basis.

Here again, the Examiner seeks to compel the Applicants to provide a sequence listing. The invention does not, however, fall within the rules requiring a sequence listing---the Applicants are stating plainly that *any* of the linkers described in the specification may be used at that position in the molecule (see in particular page 25, line 21 to page 26, line 23). Some of the linkers are not polypeptide in nature (page 26, line 20), so it is not possible to provide a sequence listing that remains consistent with the disclosure.

Rejection under Section 112. The Examiner persists in rejecting the Applicants' claims due to one passage in the working examples that noted degradation and heterogeneity in a single preparation. The Examiner seized on this part of the disclosure as indicating an unpredictable art, characterizing this as a written description issue. The Applicants stand by their prior arguments and further note the following.

First, the Applicants do provide a sufficient written description, even under the cases cited by the Examiner. In *U. of California v. Lilly*, 43 USPQ 2d 1398 (Fed. Cir. 1997), the court said that a structure or formula was sufficient for written description. Here, the Applicants' claims are defined by the formula $(X^1)_a$-F^1-$(X^2)_b$. Furthermore, the P substituents are selected from a list of sequences, and the L sequences are selected from a list of sequences, polyglycines, poly alanines and poly(Gly-Ala). Thus, the Applicants have followed the holding of *U. Calif. v. Lilly.*

Second, the degradation cited by the Examiner does not call into question the activity of the claimed molecule. The laminin-5 molecule (which includes SEQ ID NO: 131) was prepared in Example 3 (page 57), following the procedures of Example 1. The passage describing degradation reads as follows:

> Since some proteolysis was seen in laminin-5, the IC100 of laminin-5 could not be assessed accurately. All of the degradation occurred after the arginine residue (at the junction between the YIGSR repeats).

(page 57, lines 10-12). From the description, it is clear that the experiment included different numbers of laminin peptide (YIGSR) repeats linked to Fc. As all of the degradation occurred after the arginine at the junction of laminin peptide repeats, the resulting sample would include a mixture of Fc-linked molecules having different numbers of laminin peptide repeats (e.g., YIGSRYIGSRYIGSR, YIGSRYIGSRYIGSRYIGSR). The specification then notes that the IC100 could not be assessed *accurately* due to this mixture. Consistent with the rest of the specification, this passage states that Fc-linked laminin-5 was active, even if through active degradation products.[1]

Third, the Examiner repeatedly mischaracterizes the specification as "having disclosed a single species." Example 1 of the specification (page 43, line 15 to page 55, line 2) describes preparation and demonstration of activity of a molecule in which a P substituent is SEQ ID NO: 8. Although this is not itself within the scope of the amended claims (which would require SEQ ID NO: 7 to appear in the molecule), it is prepared in the same way. More important, Example 2 (page 55, line 5 to page 56, line 32) describes preparation and demonstration of activity of six molecules within the claim scope. Example 3 describes briefly the preparation of four more molecules within the claim scope (laminin-3, laminin-5, and the molecules with SEQ ID NOS: 136 and 137). The Applicants fail to see how this preparation of 10 claimed molecules and 1 related one constitute a "single disclosed species."

---

[1] The Examiner questioned the Applicants' mention of Seldane® and Claritin® in their previous response. The Applicants' argument was simply that a molecule can still be useful within the meaning of the patent statute even if it undergoes degradation. This point is made clear by the discovery that a widely marketed pharmaceutical was found to be degraded in vivo, such that the pharmaceutical was essentially an unintentional pro-drug.

Fourth, the specification itself refutes the examiner's allegations. Only one of the prepared molecules exhibited degradation and, as noted above, it was still active. The other nine molecules prepared, combined with the extensive description of how to prepare molecules of the invention, shows that the Applicants have indeed complied with the written description requirement.

The Examiner's comments regarding Claims 2 and 12 reflect a misreading of the claims. Claim 12 required that the molecule comprise "one or more sequences selected from SEQ ID NOS: 7 and 9 to 16." In its plain, unequivocal meaning, that claim requires the presence of one of those sequences 7 and 9 to 16 in the overall molecule. One molecule within the meaning of Claim 12, therefore, would include SEQ ID NO: 7. Regardless, the cancellation of Claim 2 renders this point moot.

Rejection under Section 112, second paragraph. The formulae appearing at the end of Claim 26 were included in error and are removed by the foregoing amendment.

Rejection under Section 103. In the interest of compact prosecution, the Applicants have amended the claims even though they maintain the arguments previously submitted. Claim 26 does not encompass full-length laminin nor any laminin fragment that falls outside the structures resulting from the substituent selections for P and L. The cited references do not, even in combination, suggest an Fc-YIGSR molecule. Furthermore, nothing in the cited references would lead one skilled in the art to any YIGSR repeat Fc molecule or any of the other molecules of Claim 26. For these reasons, the Applicants respectfully request the Examiner to withdraw this rejection.

Conclusion. In view of the foregoing amendments and remarks, the Applicants respectfully request reconsideration of the restriction requirement, entry of all amendments, and allowance of all claims.

Respectfully submitted,

Timothy J. Gaul
Attorney for Applicant
Registration No.: 33,111
Phone: (805) 447-2688
Date: December 23, 2005

Please send all future correspondence to:
US Patent Operations/TJG
Dept. 430, M/S 27-4-A
AMGEN INC.
One Amgen Center Drive
Thousand Oaks, California 91320-1799